Catechol-based phosphoramidites

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SUPPLEMENTARY INFORMATION

Catechol-based Phosphoramidites: A New Class of Chiral Ligands for Rhodium- Catalyzed Asymmetric Hydrogenations.

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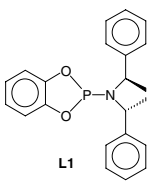
General remarks:

All reactions were performed in a dry argon atmosphere using standard Schlenk techniques. Et_2O (Na), CH_2Cl_2 (CaH) and EtOAc (boiling chips) were destilled before use. The chiral amines for **L1** – **L9** were commercially available or made by literature procedures[1]. ^{1}H-NMR, ^{13}C-NMR and ^{31}P-NMR spectra were recorded on a Varian Gemini-200 (50.32 Hz) or an Varian 300 (75.48 MHz) in $CDCl_3$. Mass spectra (HRMS) were recorded on an AEI MS-902.

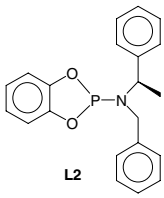
General procedure ligand synthesis:

To a solution of 1.5 g. (8.60 mmol) of *o*-phenylenephosphorochloridite and 0.87 g. (8.60 mmol) of Et_3N in 5 ml of Et_2O was added a solution of 8.60 mmol of the appropriate amine in 5 ml Et_2O at 0°C. This suspension was warmed to RT and stirred for 1.5 hrs. The reaction mixture was filtered over celite. The filtrate was concentrated. The ligand was purified by filtration over a short plug of silica gel (eluent pentane:EtOAc 10:1), yielding the ligands in 25-45% yield.



L1

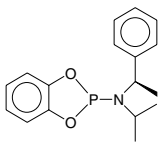
^{1}H NMR (200 MHz) δ = 7.26-7.14 (m, 12H), 7.01-6.98 (m, 2H), 4.45 (m, 2H), 1.79 (dd, *J* = 1.8, 7.1, 6H); ^{13}C NMR (50.32 MHz) δ = 146.8, 142.0, 129.1, 127.9, 127.7, 127.6, 126.9, 121.7, 53.3, 53.0, 22.4, 22.2; ^{31}P NMR (81 MHz) δ = 151.9; HRMS calculated for $C_{22}H_{22}NO_2P$ 363.138 found 363.138; $[\alpha]_D$ = -264° (c= 0.79, $CHCl_3$).



L2

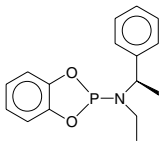
^{1}H NMR (200 MHz) δ =7.35-7.13 (m, 10H), 6.96-6.78 (m, 4H), 4.34-4.29 (m, 1H), 3.69 (ddd, *J* = 6.8, 15.7, 33.8, 2H), 1.43 (dd, *J* = 1.8, 7.1, 3H); ^{13}C NMR (50.32 MHz) δ = 146.7, 146.6, 146.5, 146.3, 141.9, 138.4, 128.5, 128.3, 128.1, 127.3, 127.2, 121.7, 111.4, 56.2, 55.9, 47.2, 47.1, 22.3, 22.1; ^{31}P NMR (81 MHz) δ =146.1; HRMS calculated for $C_{22}H_{22}NO_2P$ 349.123 found 349.122; $[\alpha]_D$ = -21° (c= 1.17, $CHCl_3$).

[1] (a) Brown, E.; Moudachirou, M. *Tetrahedron* **1994**, *50(34)*, 10309 (b) Rezai, H.; Marek, I.; Norman, J. F. *Tetrahedron* **2001**, *57(13)*, 2477 (c) Aldous, D. J.; Dutton, W. M.; Steel, P. G. *Tetrahedron: Asymmetry* **2000**, *11*, 2455



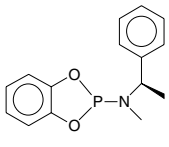
L3

^{1}H NMR (200 MHz) δ =7.42-7.22 (m, 5H), 7.04-6.95 (m, 2H), 6.90-6.81 (m, 2H), 4.43-4.37 (m, 1H), 3.18-3.05 (m, 1H), 1.54 (dd, *J* = 0.5, 7.1, 3H), 1.35 (d, *J* = 6.8, 3H), 0.96 (d, *J* = 6.8, 3H); ^{13}C NMR (50.32 MHz) δ = 146.7, 128.2, 127.6, 127.0, 121.6, 111.4, 52.5, 52.4, 46.5, 46.1, 26.3, 26.1, 25.1, 24.9, 20.7, 20.6; ^{31}P NMR (81 MHz) δ = 152.5; HRMS calculated for $C_{17}H_{20}NO_2P$ 301.123 found 301.123; $[\alpha]_D$ = +214° (c= 1.02, $CHCl_3$).



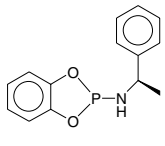
L4

^{1}H NMR (200 MHz) δ = 7.45-7.28 (m, 5H), 7.06-6.89 (m, 4H), 4.73-4.65 (m, 1H), 2.79-2.64 (m, 2H), 1.69 (dd, *J* = 1.6, 7.2, 3H), 0.89 (t, *J* = 7.1, 3H); ^{13}C NMR (50.32 MHz) δ =146.7, 146.6, 146.4, 142.3, 142.3, 128.4, 127.1, 121.6, 111.2, 55.7, 55.1, 37.2, 37.1, 21.5, 21.2, 17.0, 16.9; ^{31}P NMR (81 MHz) δ =149.5; HRMS calculated for $C_{16}H_{18}NO_2P$ 287.108 found 287.108; $[\alpha]_D$ = -65° (c= 1.36, $CHCl_3$).



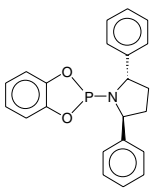
L5

^{1}H NMR (200 MHz) δ = 7.42-7.26 (m, 5H), 7.05-6.97 (m, 2H), 6.94-6.87 (m, 2H), 4.79-4.71 (m, 1H), 2.20 (d, *J* = 6.1, 3H), 1.59 (dd, *J* = 0.6, 7.0, 3H); ^{13}C NMR (50.32 MHz) δ = 146.7, 141.0, 128.4, 127.1, 121.6, 111.1, 55.0, 54.4, 26.2, 26.1, 18.8, 18.6; ^{31}P NMR (81 MHz) δ =147.0; HRMS calculated for $C_{15}H_{16}NO_2P$ 273.092 found 273.091; $[\alpha]_D$ = -28° (c= 1.09, $CHCl_3$).



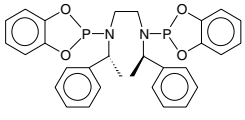
L6

^{1}H NMR (200 MHz) δ = 7.36-6.78 (m, 9H), 4.21-4.06 (m, 1H), 3.84 (m, 1H), 1.86 (d, *J* = 6.8, 3H); ^{13}C NMR (50.32 MHz) δ = 146.0, 144.5, 128.3, 126.9, 125.6, 121.8, 121.7, 111.6, 11.3, 50.0, 25.2, 25.2; ^{31}P NMR (81 MHz) δ =137.6; HRMS calculated for $C_{14}H_{14}NO_2P$ 259.076 found 259.077; $[\alpha]_D$ = -205° (c= 1.27, $CHCl_3$).



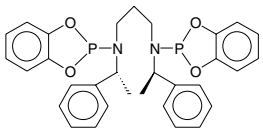
L7

^{1}H NMR (200 MHz) δ = 7.26-7.11 (m, 10H), 6.97 (d, *J* = 7.7, 1H), 6.75 (dt, *J* = 1.1, 7.7, 1H), 6.51 (dt, *J* = 1.1, 7.7, 1H), 5.95 (d, *J* = 7.7, 2H), 2.36-2.25 (m, 2H), 1.67-1.57 (m, 2H); ^{13}C NMR (50.32 MHz) δ =145.0, 128.1, 126.8, 126.1, 121.6, 121.2, 111.5, 110.3, 63.2, 63.1, 33.7; ^{31}P NMR (81 MHz) δ =143.9; HRMS calculated for $C_{22}H_{20}NO_2P$ 361.122 found 361.123; Anal. Calc. for $C_{22}H_{20}NO_2P$: C, 73.12 %; H, 5.58 %; N, 3.88 %, found : C, 73.09 %; H, 5.58 % ; N, 3.89 %; $[\alpha]_D$ = -104° (c= 0.79, $CHCl_3$).



L8

^{1}H NMR (200 MHz) δ = 7.40-7.15 (m, 10H), 7.00-6.84 (m, 8H), 4.24-4.13 (m, 2H), 2.74-2.43 (m, 4H), 1.26 (d, *J* = 7,1 Hz, 6H); ^{13}C NMR (50.32 MHz) δ = 146.6, 141.7, 128.3, 127.2, 121.8, 111.5, 111.3, 55.2, 54.8, 44.5, 44.3, 20.5, 20.3; ^{31}P NMR (81 MHz) δ =150.1; HRMS calculated for $C_{30}H_{30}N_2O_4P_2$ 544.168 found 544.168; $[\alpha]_D$ = -125° (c= 1.06, $CHCl_3$).



L9

^{1}H NMR (200 MHz) δ = 7.43-7.25 (m, 10H), 7.00-6.82 (m, 8H), 4.40-4.29 (m, 2H), 2.32-2.15 (m, 4H), 1.49 (dd, *J* = 1,71, 7.0, 6H), 1.53-1.21 (m, 4H); ^{13}C NMR (50.32 MHz) δ = 146.0, 141.8, 128.4, 127.2, 127.1, 121.7, 111.2, 55.5, 55.0, 40.3, 40.2, 31.8, 21.5, 21.2; ^{31}P NMR (81 MHz) δ =148.5; HRMS calculated for $C_{31}H_{32}N_2O_4P_2$ 558.184 found 558.184; $[\alpha]_D$ = +79° (c= 1.41, $CHCl_3$).

General procedure hydrogenations:

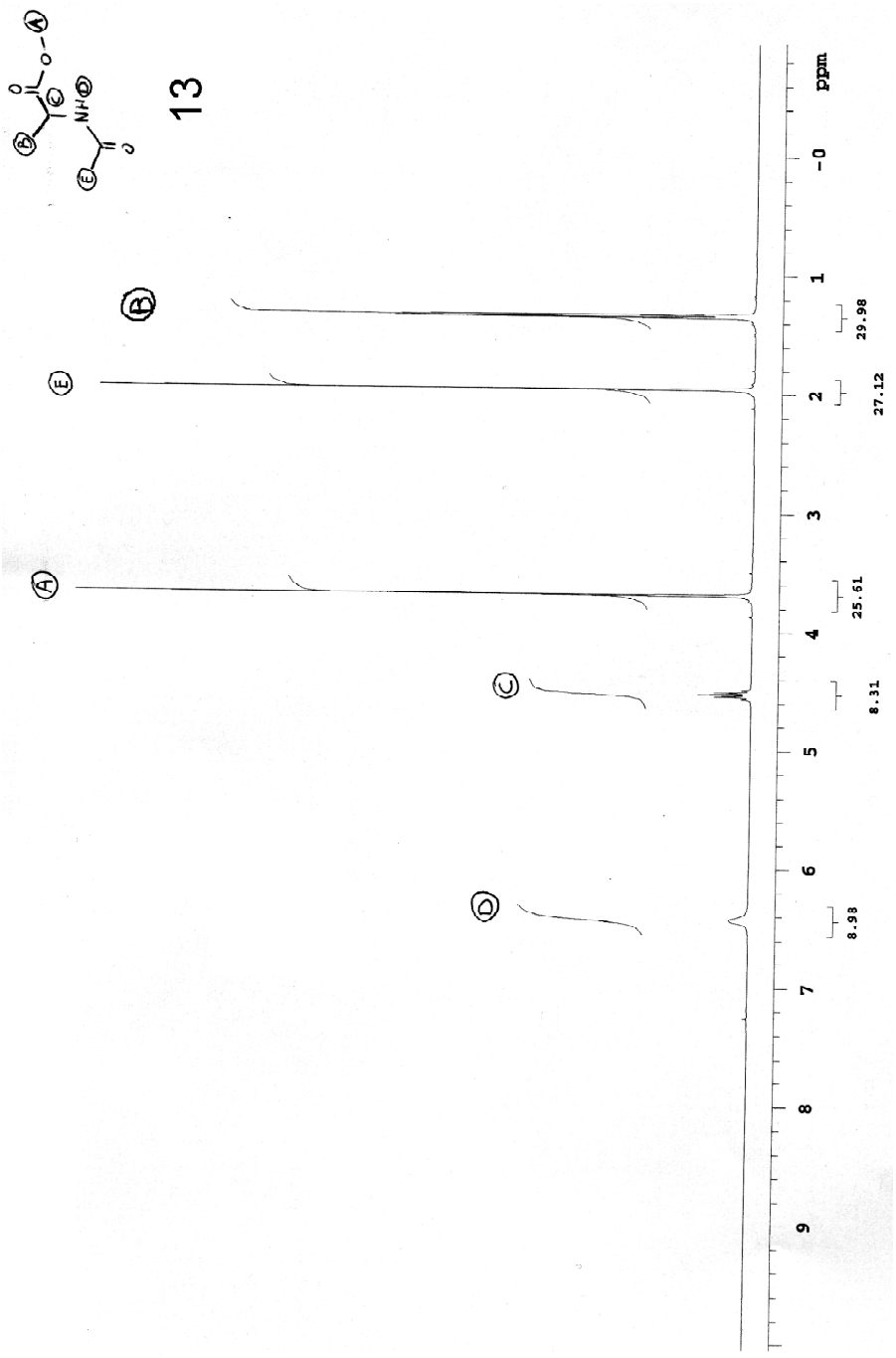
In a glass tube, 0.81 mg (2 µmol) of $Rh(COD)_2BF_4$, 4 µmol of ligand (2 µmol in case of the bidentate ligands **L8** and **L9**), 200 µmol of the substrate and 4 ml of solvent, was added. This small glass tube was placed in a semi-automated autoclave with eight reactors (Endeavor) that was purged 4 times with nitrogen and once with hydrogen. Then, the autoclave was pressurized with 5 or 25 bar of hydrogen. The reaction was stirred for 16 hours. A sample of the resulting mixture was filtered over a silica plug and subjected to conversion (^{1}H NMR) and e.e. determination (capillary GC). Full conversion was observed in most cases. As typical examples the isolated yields for **13**, **15**, **16** and **26** were determined. The complete reaction mixtures were filtered over a short silica plug (EtOAc) to yield the corresponding products in 99% yield. The ^{1}H NMR's of the products are added at the end of the SI. Absolute configurations were determined by comparison with reference compounds (**26**, **27**, **31**), literature values (GC or HPLC injections; **6**, **12**, **13**, **14**, **15**, **16**, **29**),[2a,b,c] optical rotation (**28**)[2d] or assigned by analogy through chiral GC elution order (**30**, **32**).

Entry	Compound	Method*	Retention time (minutes)	Retention time (minutes)
1	**6**	A	6.7 (R)	7.1 (S)
2	**12**	B	12.8 (R)	14.9 (S)
3	**13**	C	3.4 (R)	3.9 (S)
4	**14**	D	11.5 (S)	11.7 (R)
5	**15**	E	15.8 (S)	16.7 (R)
6	**16**	F	39.4 (S)	41.0 (R)
7	**26**	G	12.8 (S)	13.9 (R)
8	**27**	H	15.8 (S)	16.7 (R)
9	**28**	H	13.5 (S)	14.6 (R)
10	**29**	E	9.0 (S)	9.5 (R)
11	**30**	I	12.1 (S)	12.7 (R)
12	**31**	E	14.0 (S)	15.4 (R)
13	**32**	E	17.0 (S)	17.6 (R)

* Methods A, C-I are GC methods and method B is HPLC method

[2] (a) Van den Berg, M.; Minnaard, A. J.; Haak, R. M.; Leeman, M.; Schudde, E. P.; Meetsma, A.; Feringa, B. L.; de Vries, A. H. M.; Maljaars, C. E. P.; Willans, C. E.; Hyett, D.; Boogers, J. A. F.; Henderickx, H. J. W.; de Vries, J. G. *Adv. Synth. Catal.* **2003**, *345*, 308 (b) Van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; Van Esch, J.; De Vries, A. H. M.; De Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539 (c) Peña, D.; Minnaard, A. J.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 14552 (d) Choi, Y. K.; Kim, M. J.; Ahn, Y.; Kim, M-J. *Org. Lett.* **2001**, *3*, 4099

Method A: CP Chiralsil-L-Val from Chrompack (30m x 0.25mm x 0.12μm), 160°C
Method B: Chiralcel-OD (0.46 cm x 25 cm), *i*-PrOH: heptane 1:9
Method C: CP Chiralsil-L-Val from Chrompack (30m x 0.25mm x 0.12μm), 110°C
Method D: CP Chiralsil-Dex CB from Chrompack (25m x 0.25mm x 0.25μm), 160°C
Method E: CP Chiralsil-Dex CB from Chrompack (25m x 0.25mm x 0.25μm), 170°C
Method F: CP Chiralsil-Dex CB from Chrompack (25m x 0.25mm x 0.25μm), 130°C
Method G: CP Chiralsil-Dex CB from Chrompack (25m x 0.25mm x 0.25μm), 100°C
Method H: CP Chiralsil-Dex CB from Chrompack (25m x 0.25mm x 0.25μm), 140°C
Method I: CP Chiralsil-Dex CB from Chrompack (25m x 0.25mm x 0.25μm), 150°C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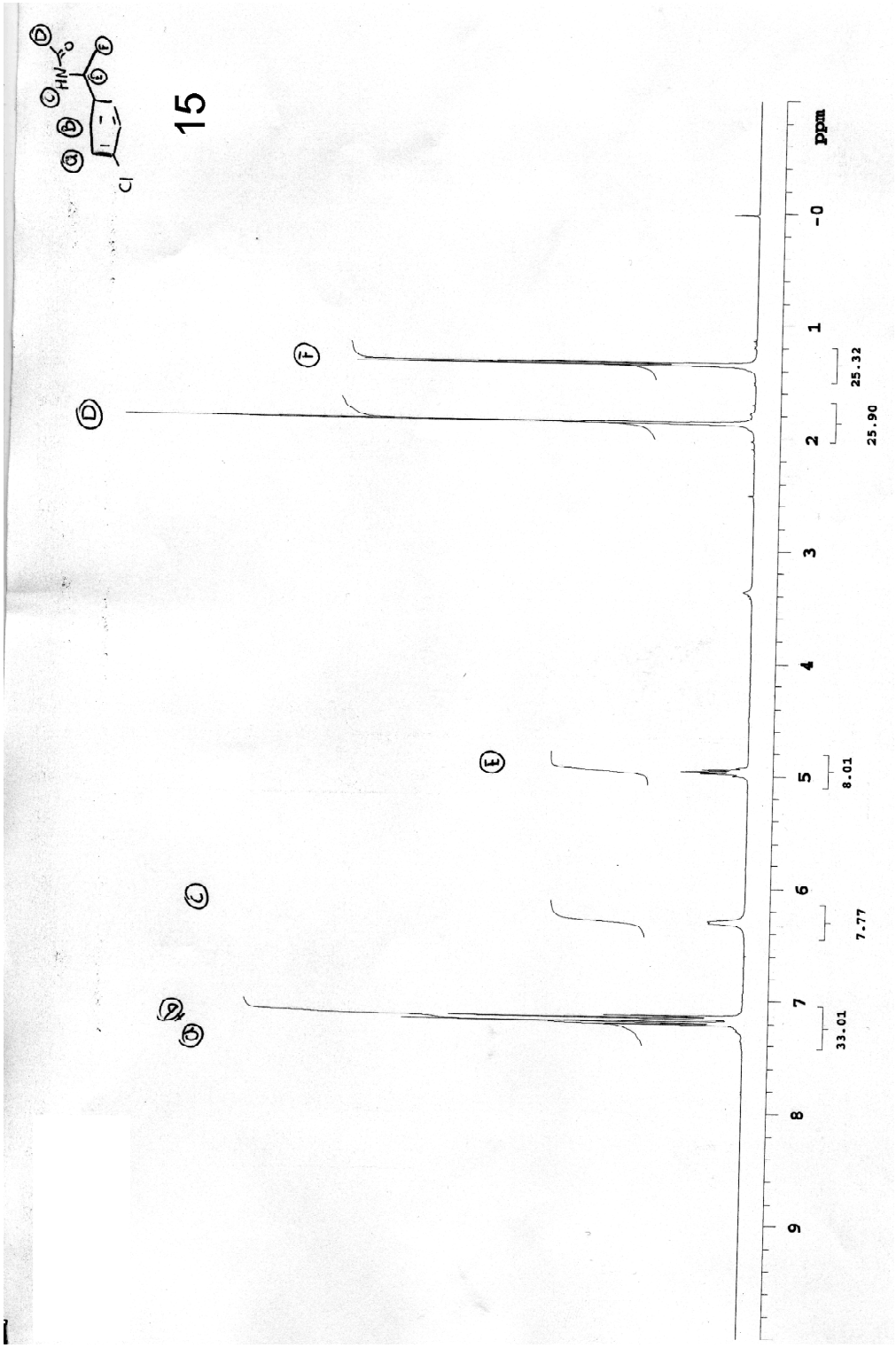
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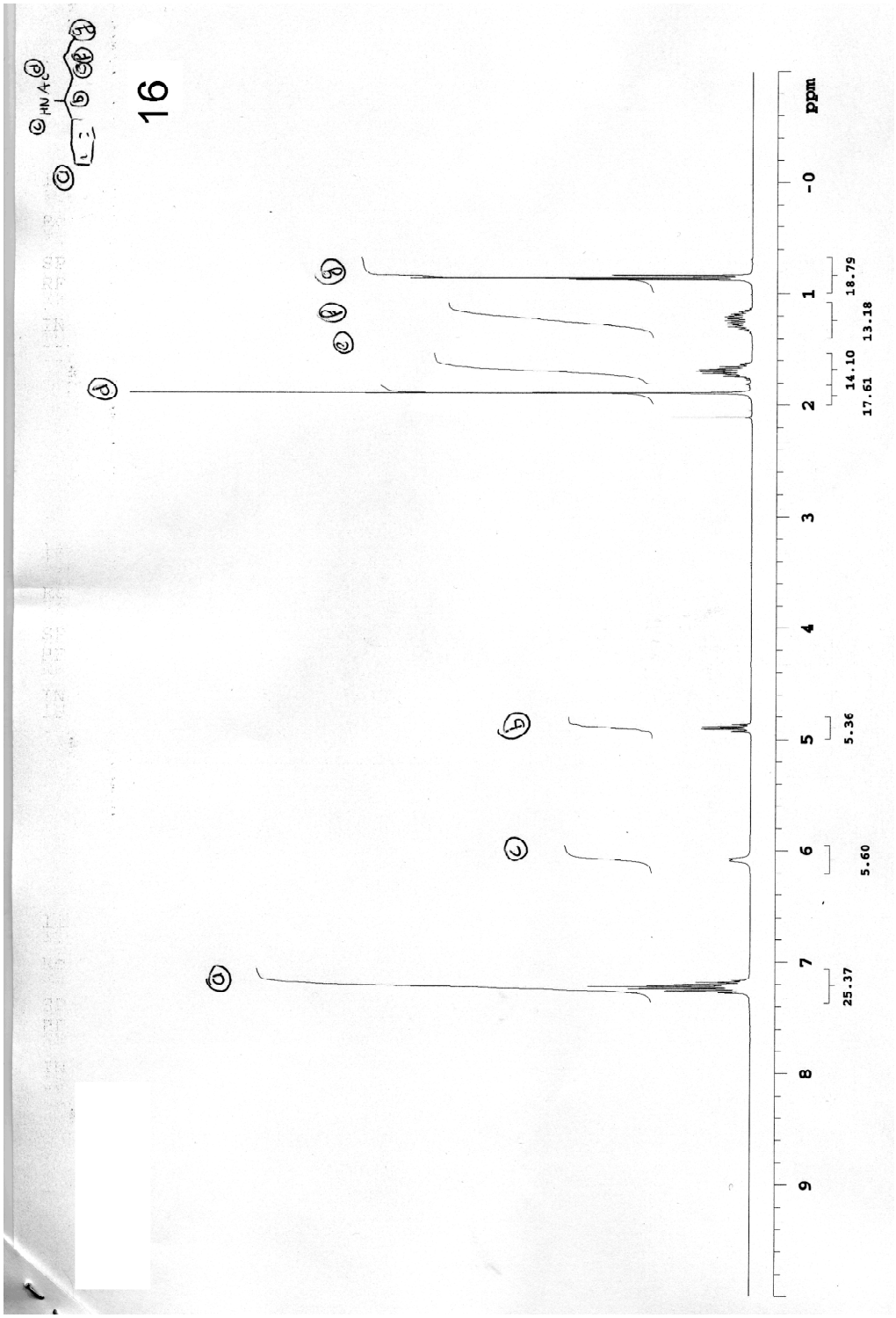
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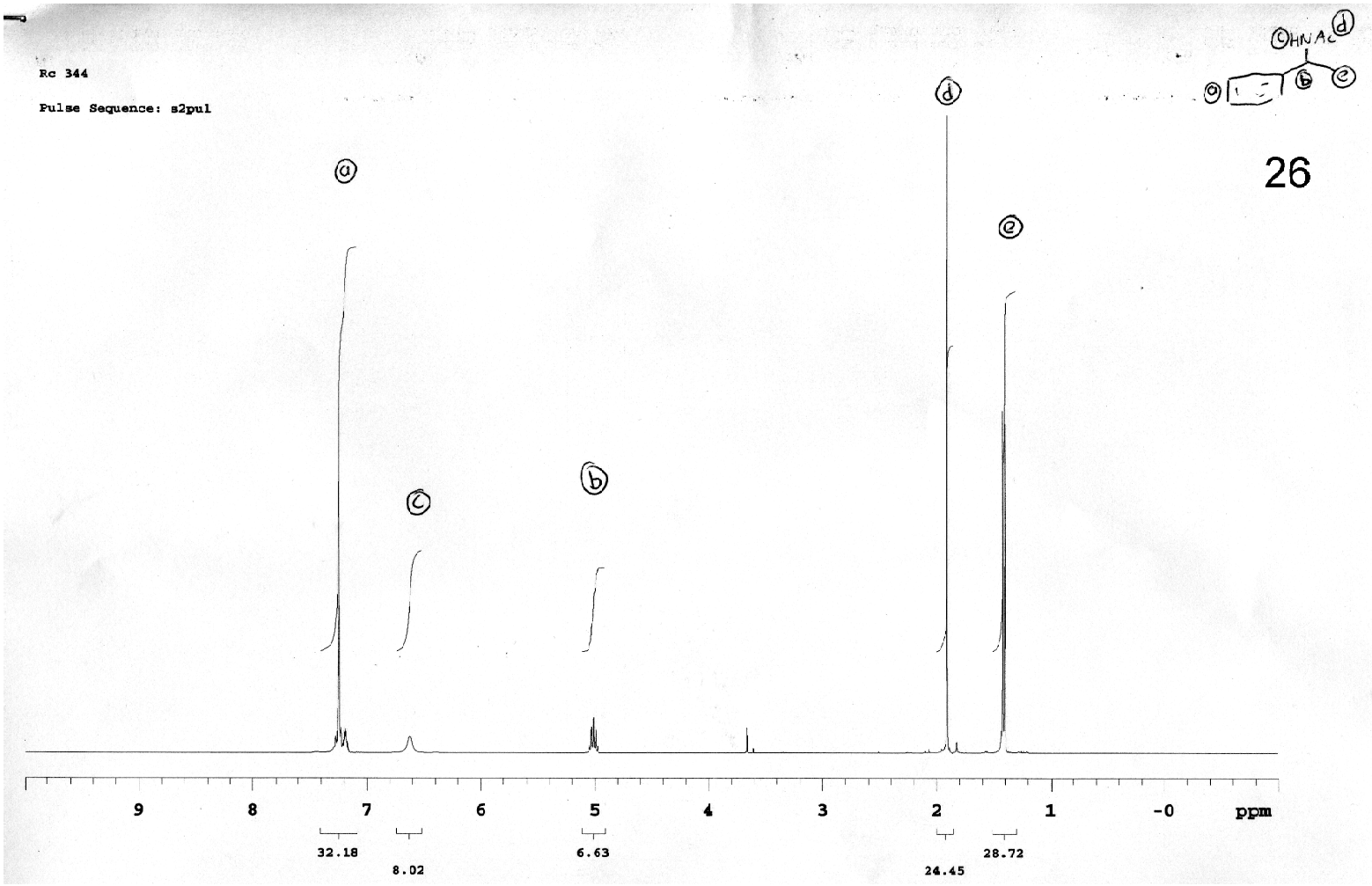
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